The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte D. WADE WALKE,
CARL JOHAN FRIDDLE,
BRIAN MATHUR, and
C. ALEXANDER TURNER, JR.

MAILED
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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Appeal No. 2005-1285
Application No. 09/893,321

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-6, all of the claims remaining. Claim 1 is representative and reads as follows:

> 1. An isolated nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence drawn from the group consisting of SEQ ID NOS: 2 and 4.

Claims 1-6 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility. We reverse the examiner's rejection and enter a new rejection of claims 3 and 4.

Background

"GABA receptors bind potent inhibitory neurotransmitters and this interaction serves as a target for a variety of pharmaceutically active agents such as benzodiazepines, barbiturates, and alcohol." Page 1. The specification discloses "human polynucleotides encoding proteins that share sequence similarity with animal gamma-amino butyric acid (GABA) receptor subunits." Id. More specifically, the encoded protein is similar in sequence to the GABA receptor gamma subunit. See page 16: "[t]he described sequences share structural similarity with GABA receptor proteins, and particularly GABA A receptor gamma-1, -2, and -3, -4, -5, and -6 subunits."

The specification refers to the protein generically as a "novel human protein" or NHP. "[T]he present invention also relates to processes for identifying compounds that modulate, i.e., act as agonists or antagonists, of NHP expression and/or NHP activity that utilize purified preparations of the described NHPs and/or NHP product, or cells expressing the same. Such compounds can be used as therapeutic agents for the treatment of any of a wide variety of symptoms associated with biological disorders or imbalances." Page 3.

Discussion

Claim 1 is directed to a nucleic acid molecule encoding either SEQ ID NO:2 or SEQ ID NO:4. (SEQ ID NO:4 is a truncated version of SEQ ID NO:2.) The examiner rejected all of the pending claims for lack of patentable utility.

We start, as usual, with Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). The claimed invention in Brenner "a chemical process which yields an already

known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693.

The Brenner Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court of Customs and Patent Appeals first applied Brenner in In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, the Federal Circuit held that § 101 was not satisfied by a disclosure that "solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" In re Ziegler, 992 F.2d 1197, 1203, 26 USPQ2d 1600, 1605 (Fed. Cir. 1993). "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. "[A]t best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980), where the claimed pharmaceutical compositions were disclosed to be useful in treating acute myeloblastic leukemia. The active ingredients in the compositions were closely related to compounds which were "well recognized in the art as valuable for use in cancer chemotherapy" and the evidence showing that the claimed compositions were effective in treating tumors in a mouse model. See id. at 1323-24, 206 USPQ at 887-88.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in some circumstances, in vitro testing is sufficient to show utility. In Cross, the evidence showed successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds. The court held that the evidence was sufficient to meet the requirements of § 101. Id. at 1051, 224 USPQ at 748.

Finally, in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), the Federal Circuit held that § 101 was satisfied by disclosure that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity

and evidence of in vivo activity against tumors in a mouse model. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from these cases. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, a steroid compound that is useful as an object of scientific inquiry, and polypropylene that is useful for pressing into a flexible film, both lack sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. Under this standard, § 101 is satisfied by pharmaceutical compositions useful for treating leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a known, related compound (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" do not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55. Likewise, disclosing polypropylene that is "plastic-like" and can be pressed into a flexible film showed that the applicant was "at best . . .

on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See Brana, 51 F.3d at 1566, 34 USPQ2d at 1441 ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

In this case, the examiner has concluded that the specification does not disclose a patentable utility for the claimed nucleic acids. See the Examiner's Answer, page 3. The examiner characterizes the claimed protein as "what is termed an 'orphan receptor' in the art," (id., page 4) because the specification does not disclose "the natural ligands or biological significance" of the encoded protein. Page 6.

The examiner argues that the specification's disclosure that the encoded protein is similar to animal GABA receptors does not establish its utility because "[n]o comparisons between the sequence of the protein of the present invention and any GABA protein has been disclosed in the specification, nor does the specification disclose that the protein . . . has biological activities similar to GABA proteins." Page 5. The examiner argues that "[s]equence homology is seldom sufficient in the absence of supporting evidence, because the relevant literature acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence

databases." Id. The examiner cites Skolnick,[1] Bork 2000,[2] Doerks,[3] Smith,[4] Brenner,[5] and Bork 1996,[6] as supporting this position.

Appellants argue that those skilled in the art would accept the evidence of record as showing that the protein encoded by the claimed nucleic acids is likely to be a gamma subunit of a GABA receptor. See the Appeal Brief, pages 7-17. Appellants also argue that GABA receptors have well-known biological activities, which include "serv[ing] as a target for a variety of pharmaceutically active agents such as benzodiazepines, barbiturates, and alcohol," as disclosed in the specification. Thus, Appellants conclude, those skilled in the art would recognize that the protein encoded by the claimed nucleic acids would be useful for the same purposes as other GABA receptors. Appeal Brief, page 7.

We agree with Appellants that the evidence in this case does not support the examiner's rejection. First, we cannot agree with the examiner that those skilled in the art would consider the evidence insufficient to show that the claimed nucleic acids encode a GABA receptor gamma subunit. As we noted above, the initial burden of showing lack of utility is on the examiner. See Brana, 51 F.3d at 1566, 34 USPQ2d at 1441. See also In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974)

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[1] Skolnick et al., "From genes to protein structure and function: novel applications of computational approaches in the genomic era," Trends Biotechnol., Vol. 18, pp. 34-39 (2000).
[2] Bork, "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle," Genome Research, Vol. 10, pp. 398-400 (2000).
[3] Doerks et al., "Protein annotation: detective work for function prediction," Trends in Genetics, Vol. 14, No. 6 pp. 248-250 (1998).
[4] Smith et al., "The Challenges of Genome Sequence Annotation or 'The devil is in the details'," Nature Biotechnology, Vol. 15, pp.1222-1223 (1997).
[5] Brenner, "Errors in Genome Annotation," Trends in Genetics, Vol. 15, No.4, pp. 132-133 (1999).
[6] Bork et al., "Go hunting in sequence databases but watch out for the traps," Trends in Genetics, Vol. 12, No. 10, pp. 425-427 (1996).

("[A] specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope.").

In this case, that means that the burden is on the examiner to show that those skilled in the art would doubt the objective truth of the specification's statement that the claimed nucleic acids encode a GABA receptor gamma subunit. The examiner cited several scientific papers that, collectively, show two things: (1) comparing a new protein with existing sequences does not always accurately predict the function of the new protein and (2) minor changes in amino acid sequence can result in major changes in a protein's function. The examiner characterizes these references as showing "that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases." Examiner's Answer, page 5.

In our view, the references cited by the examiner show that sequence similarity does not always accurately predict function, because of potential inaccuracies in the sequence databases and because function does not necessarily follow from a limited amount of similarity. However, the evidence does not support a bright-line rule that structural similarity by itself cannot accurately predict function. Each case must be considered on its own facts.

Here, the evidence shows that the protein encoded by the claimed nucleic acids is more than 99% identical to a protein characterized by those in the art as a human

GABA receptor gamma subunit.[7] Specifically, Ymer[8] discloses a human "$GABA_A$ receptor γ_1 subunit." See the abstract. The amino acid sequence of the protein is shown in Ymer's Figure 2: the sequence differs from that of instant SEQ ID NO:2 in only a single position (position 145 is isoleucine in SEQ ID NO:2 and the corresponding position is valine in Ymer's sequence).

In light of the extensive sequence similarity between SEQ ID NO:2 and Ymer's sequence and Ymer's unqualified characterization of the protein as a human $GABA_A$ receptor γ_1 subunit, we agree with Appellants that those skilled in the art would have recognized that the protein encoded by SEQ ID NO:2 is likely to be a GABA receptor gamma subunit, as disclosed in the specification. The evidence of record shows that the general problems discussed in the examiner's references are not applicable to the presently claimed nucleic acids.

Ymer also discloses that GABA receptors that include different gamma subunits have different pharmacological properties. See page 3261, right-hand column ("We show that this γ variant . . ., when assembled with α_1 and β_1 subunits, participates in the formation of $GABA_A$/benzodiazepine receptors whose pharmacological properties differ in important aspects from receptors containing the γ_2 subunit."). The examiner has not challenged the specification's statement that GABA receptors are "a target for a variety of pharmaceutically active agents such as benzodiazepines, barbiturates, and alcohol."

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[7] Appellants cite a GenBank record as evidence on this point. We decline to give any weight to the GenBank record or the publication cited therein because both appear to reflect a post-filing date state of the art. The instant application claims priority to June 27, 2000, while the GenBank record states that it was created Feb. 28, 2003, based on a publication from 2002.

[8] Ymer et al., "Structural and functional characterization of the γ_1 subunit of $GABA_A$/benzodiazepine receptors," EMBO Journal, Vol. 9, No. 10, pp. 3261-3267 (1990). Ymer was cited in the IDS filed August 16, 2002 and applied by the examiner in the Office action mailed March 10, 2003.

We conclude that the evidence of record does not support the examiner's rejection. Specifically, in view of the evidence that the claimed nucleic acids encode a GABA receptor gamma subunit and the evidence that gamma subunits affect the pharmacological properties of GABA receptors, the examiner has not adequately explained why a person of ordinary skill in the art would not have found the protein encoded by the claimed nucleic acids to be useful for, at least, identifying agonists or antagonists of GABA receptors that could be expected to have activities similar to known benzodiazepine or barbiturate drugs.

We reverse the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility. We note, however, that our decision is based on the expected function of the encoded protein as a GABA receptor gamma subunit, and not on the uses that are asserted on pages 17-24 of the Appeal Brief.

New Ground of Rejection

Under the provisions of 37 CFR § 41.50(b), we enter the following ground of rejection: Claims 3 and 4 are rejected under 35 U.S.C. § 102(b) as anticipated by Ymer.

Claims 3 and 4 read as follows:

3. An isolated nucleic acid molecule comprising at least 80 contiguous bases of nucleotide sequence of SEQ ID NO:1.

4. An isolated nucleic acid molecule comprising at least 80 contiguous bases of nucleotide sequence of SEQ ID NO:3.

Thus, claims 3 and 4 read on any nucleic acid molecule that comprises 80 bases of the sequences shown in SEQ ID NOs 1 and 3, respectively.

As discussed above, Ymer discloses the γ_1 subunit of human $GABA_A$ receptor. Ymer teaches that

> [t]he γ_1 subunit cDNA was isolated . . . by screening human, bovine and rat brain libraries with a degenerate oligonucleotide probe. . . . Novel subunit cDNAs were classified as γ_1, γ_2 and δ subunit cDNAs on the basis of their encoded polypeptide sequences. Figure 1 presents the nucleotide and deduced amino acid sequence of the rat γ_1 subunit cDNA. The human, bovine and rat γ_1 polypeptides are compared with each other . . . in Figure 2. The γ_1 cDNAs of all three species encode polypeptides of 465 amino acids.

Paragraph bridging pages 3261 and 3262.

Thus, Ymer teaches that a full-length cDNA was isolated from a human brain cDNA library, sequenced, and deduced to encode the amino acid sequence shown in Ymer's Figure 2. The nucleotide sequence of the human cDNA is not disclosed, but must have been at least 1395 bases long (in order to encode 465 amino acids). Thus, the evidence shows that

(1) Both Ymer's cDNA and the cDNA of SEQ ID NOs 1 and 3 were isolated from human brain cDNA libraries. See the passage from Ymer quoted above and the instant specification at page 16 ("The NHP nucleotides were obtained from clustered human sequences and cDNA isolated from a human brain cDNA library."); and

(2) Ymer's cDNA and the cDNAs of SEQ ID NOs 1 and 3 encode amino acid sequences that are identical in all but one position (the position corresponding to amino acid 145 in SEQ ID NOs 2 and 4).

Based on this evidence, it is reasonable to conclude that the human cDNA disclosed by Ymer shares at least 80 contiguous bases of sequence with SEQ ID NOs 1 and 3 of this application. That is, since Ymer's cDNA was isolated from the same tissue type as the cDNA represented by SEQ ID NOs 1 and 3 and encodes an amino acid sequence that is identical in all but one position out of 465 (for SEQ ID NO:1, encoding SEQ ID NO:2) or 256 (for SEQ ID NO:3, encoding SEQ ID NO:4), it is reasonable to

conclude that at least 80 contiguous bases of Ymer's 1395 bp cDNA are identical to the cDNA of instant SEQ ID NOs 1 and 3, encoding SEQ ID NOs 2 and 4, respectively.

"It is well settled that a claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." Celeritas Techs. Ltd. v. Rockwell Int'l Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522 (Fed. Cir. 1998). "An inherent structure, composition or function is not necessarily known. . . . Insufficient prior understanding of the inherent properties of a known composition does not defeat a finding of anticipation." Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

"When the claimed compositions are not novel they are not rendered patentable by recitation of properties, whether or not these properties are shown or suggested in the prior art." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). "In response to the PTO's asserted prima facie case the applicant may argue that the inference of lack of novelty was not properly drawn, for example if the PTO did not correctly apply or understand the subject matter of the reference, or if the PTO drew unwarranted conclusions therefrom. However, when the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." Spada, 911 F.2d at 708, 15 USPQ2d at 1658.

We conclude that a preponderance of the evidence shows that Ymer's cDNA inherently meets the limitations of claims 3 and 4 and therefore anticipates them. "[A]fter the PTO establishes a prima facie case of anticipation based on inherency, the burden shifts to appellant to 'prove that the subject matter shown to be in the prior art

does not possess the characteristic relied on.'" In re King, 801 F.2d 1324, 1327, 231 USPQ 136, 138 (Fed. Cir. 1986).

Time Period for Response

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .

(2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

REVERSED; 37 CFR § 41.50(b)

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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EG/jlb

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